REMARKS/ARGUMENTS

Claim 32 is canceled hereby. Claims 1-31 and 33-139 remain pending herein. Claims 1-17 and 45-139 have been withdrawn from consideration by the U.S. PTO. New claim 140 is added hereby.

In the March 24, 2006 Office Action, claims 18-44 were rejected under 35 U.S.C. §112, second paragraph.

The Office Action contains objections to the expressions "derivatives of said compounds", "metabolites of said compounds", "analogues of said compounds", "mimic molecules", "precursor molecules of circiliol", "derivatives of circiliol", "metabolites of circiliol", "analogues of circiliol", and "mimic molecules".

The amendments to the claims as set forth above include the deletion of all of the above-noted expressions.

The March 24, 2006 Office Action also contains an objection to the expression "substantially simultaneously" in claim 26. In response, claim 26 has been amended to replace the expression "substantially simultaneously" with the expression "essentially simultaneously", the latter expression being defined in the specification, paragraph 119.

Accordingly, it is respectfully requested that the U.S. PTO reconsider and withdraw this rejection.

Claims 18-44 were rejected under 35 U.S.C. §112, first paragraph. The March 24, 2006 Office Action contains a statement that the specification is enabling for the treatment of lung cancer and pancreatic cancer, but does not reasonably provide enablement for the treatment of neoplasia in general.

The amendments to the claims as set forth above include limiting the scope of treatment from patients suffering from neoplasia to patients suffering from pancreatic cancer

or lung cancer. Accordingly, the present claims have been amended to recite only the subject matter acknowledged by the U.S. PTO as being supported by an enabling description in the present specification. Accordingly, it is respectfully requested that the U.S. PTO reconsider and withdraw this rejection.

Claims 18-27, 30-33, and 37-44 were rejected under 35 U.S.C. §103(a) over WO 00/03706 (Francis '706) in view of WO 99/01118 (Chinery '118), further in view of Tsukada et al.

Francis '706 discloses a broad sprectrum of flavonoids, but merely refers to the flavonoids as having an effect on the clonogenic cell population in the tumor. Furthermore, Francis '706 gives no suggestion of using circiliol with a chemotherapeutic agent for the treatment of pancreatic cancer or lung cancer.

Circiliol is presented as a potent inhibitor of the enzyme arachidonic 5 -lipoxygenase, which has been well published in the literature. Tsukada asserts that circiliol exhibits potent antiproliferative effects on human leukemia cells. The present invention does not relate to the use of circiliol as an antiproliferative agent for leukemia cells, as the present inventor, like others before him, demonstrated that this compound is only moderately active as a anticancer agent and has never been brought forward for cancer therapy even though its antiproliferative effects have been published since the mid-80s.

The present inventor observed that when used as an anti-viral agent against picornaviruses, the flavone circiliol, unlike other flavones (e.g., Eupatorin), had the unique ability to prevent the viral RNA or DNA from exiting the infected cells. It was this observation relating to circiliol alone and realizing that certain antivirals and antineoplastic agents have a core chemical structure based on being analogues of the DNA and RNA bases, one such agent being 2-deoxy-2-2-difluorocytidine (gemcitabine), that prompted the present

inventor to test his hypothesis that if a therapeutic agent resembling a DNA or RNA molecule should be applied in association with this specific flavone (circiliol), the therapeutic index of the nucleotide should be enhanced because they would be retained or trapped within the treated cells. This is a unique effect of circiliol which is not demonstrated by other flavones, and by preventing escape of gemcitabine or other chemo agents, a unique combination is obtained (in the case of circiliol and gemcitabine, a one log increase is obtained in the therapeutic index of gemcitabine.

Chinery et al (WO/9901118) discloses an antioxidant enhancement of therapy for hyperproliferative conditions. Circiliol is not documented anywhere in the scientific literature as an antioxidant. Chinery asserts that antioxidants induce cell cycle arrest and apoptosis in abnormally proliferating cells.

Circiliol has never been documented in the scientific literature to induce cell cycle arrest and apoptosis in abnormally proliferating cells. Chinery's definition of antioxidants includes but is not limited to the following classes of compounds: (H) inhibitors of lipoxygenases and cyclooxygenases.

Any assumption that all flavonoids which include all the chemical groups (flavones, flavanones, isoflavones, coumarins and chalcones) that inhibit any of the many different lipoxygenase enzymes all act as antioxidants is incorrect, as published papers document that polymethoxylated flavonoids like circiliol are virtually inactive as scavengers of the diphenylpicrylhydrazyl radical, a common test of antioxidant activity (see, e.g., Inhibitors of 15-lipoxygenase from orange Peel. Journal of Agric. Food Chem. 2000 Nov, 48 (11): 5576-80.)

In view of the above, no combination of Francis '706, Chinery '118 and Tsukada would suggest the subject matter within the scope of the present claims.

Accordingly, it is respectfully requested that the U.S. PTO reconsider and withdraw this rejection.

Claim 28 was rejected under 35 U.S.C. §103(a) over Francis '706 in view of Chinery '118 and Tsukada et al., further in view of U.S. Patent No. 6,608,026 (Wang '026).

Wang '026 is relied on by the U.S. PTO for alleged disclosure of a combination therapy which involves the use of radiation. Any such disclosure in Wang '026 would not overcome the shortcomings of Francis '706, Chinery '118 and Tsukada as attempted to be applied against claim 18, from which claim 28 depends. Accordingly, it is respectfully requested that the U.S. PTO reconsider and withdraw this rejection.

Claims 29 and 34-36 were rejected under 35 U.S.C. §103(a) over Francis '706 in view of Chinery '118 and Tsukada, further in view of U.S. Patent No. 6,569,853 (Borisy '853).

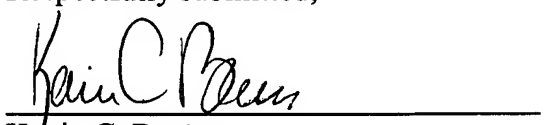
Borisy '853 is relied on in the Office Action for alleged disclosure of a method of treating a cancer patient which may be performed alone or in conjunction with another therapy such as surgery, radiation or chemotherapy, and that the formulations for oral use include tablets which may be coated or adapted not to release the active drug substance until after passage of the stomach. Any such disclosure in Borisy '853 would not overcome the shortcomings of Francis '706, Chinery '118 and Tsukada as attempted to be applied against claim 18, from which claims 29 and 34-36 each ultimately depend. Accordingly, it is respectfully requested that the U.S. PTO reconsider and withdraw this rejection.

In view of the above, claims 18-31, 33-44 and 140 are in condition for allowance.

If the Examiner believes that contact with Applicants' attorney would be advantageous toward the disposition of this case, the Examiner is herein requested to call Applicants' attorney at the phone number noted below.

The Commissioner is hereby authorized to charge any additional fees associated with this communication or credit any overpayment to Deposit Account No. 50-1446.

Respectfully submitted,



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